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COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,996	ECKER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/24/03; 7/12/04; 12/27/05;
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. While this application claims priority to a variety of parent applications, certain claims are not supported by the earliest parent applications, such as 09/798,007. For example, claim 3, drawn to air samples, appears to lack any support in 09/798,007. Similarly, claims 18 and 19 appear to lack support in the parent applications.

Claim Interpretation

2. As a preliminary issue, the claims must be interpreted before proceeding with the prior art analysis. First, what is the meaning of the phrase "wherein both first and second bioagent identifying amplicons are correlative". The specification discusses this term at page 12, lines 6-8. However, this definition appears to simply require that the "corrleative amplicons" are amplified by the same primers. The claims will be interpreted in this light. Second, the phrase "molecular mass" appears repeatedly in the claims and specification but no definition of this term was found. Therefore, the term is broadly read to encompass any mode of determination of molecular mass, including mass determinations by sizing on gel electrophoresis, as well as mass spectrometry, which is the clearly preferred mode of analysis.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, 4-7, 11, 17, 20, 21 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Hurst et al (Anal. Chem. (1998) 70:2693-2698).

Hurst teaches a method of claims 1 and 20 of identifying a bioagent in sample (see page 2696, column 1), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 2695, table I, and page 2694, column 2, where primers were synthesized which amplified a conservative region of the pmoA gene from methanotrophs and see figures 2-4 where molecular mass is shown for bioagents)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figure 4 and page 2696, where the MALDI-TOF can distinguish different microorganisms amplified by the 56 base pair regions).

With regard to claims 2, 4, 5, Hurst teaches environmental samples including groundwater and soil samples (see page 2693, column 1).

With regard to claims 6, 7, Hurst teaches obtaining surface swab samples from a container in a building (see page 2694, column 2 "Chromosomal DNA was isolated from methanotrophic cultures grown on agarose plates.", where the plates are the container and are in a building.

With regard to claims 11, 21, Hurst teaches analysis of separate PCRs (see page 2696, column 1) followed by comparison of the results (see figure 2) which comparison

necessarily utilized a computer database that stored the spectra and generated figure 2, and where the data was stored in the computer database.

With regard to claim 17, 27, Hurst teaches analysis of methanotrophic bacteria (see abstract).

With regard to claim 20, Hurst expressly discusses analysis of bioremediation processes (see page 2693, column 1).

5. Claims 1, 6, 7, 11, 14-17, 20, 21 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Muddiman et al (Anal. Chem. (1996) 68:3705-3712).

Muddiman teaches a method of claims 1 and 20 of identifying a bioagent in a sample (see abstract), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 3707, column 1, where the are drawn to the 16S and 23S rRNA sequences, which are variable at some level at those locations and page 3707, column 2)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figures 2,-5 where the masses of two different species are compared).

With regard to claims 6 and 7, Muddiman teaches samples in a container in a building (see page 3707, column 1).

With regard to claim 11, 21, Muddiman teaches analysis of separate PCRs followed by comparison of the results (see figures 2-5) which comparison necessarily

utilized a computer database that stored the spectra and generated figure 2, and where the data was stored in the computer database.

With regard to claims 14-15, 24, 25, Muddiman uses FT-ICR mass spectrometry with ESI (see page 3707, column 2).

With regard to claims 16, 26, the spectra of Muddiman show the presence or absence of the organisms, which provides some measurement of quantity (see figures 2-5).

With regard to claim 17, 27, Muddiman teaches that the bioagent is a Bacilli bacterium (see abstract).

6. Claims 1, 2, 4-9, 11, 17, 20, 21 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Lupski et al (U.S. Patent 5,523,217).

Lupski teaches a method of claims 1 and 20 of identifying a bioagent in a sample (see abstract), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see column 7, lines 25-35, where Lupski teaches using a pair of primers to extend and measure extension products by size)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see column 7, lines 25-35, where Lupski teaches comparison of size patterns).

With regard to claims 2, 4-9, Lupski teaches analysis of environmental samples including water and soil samples (see column 10, lines 8-67), swabs and samples in

buildings and containers (see column 11, lines 20-30 and lines 1-12), and foodstuff samples (see column 10, lines 50-58).

With regard to claims 11, 21, Lupski expressly teaches the use of databases and comparison of moleculer masses by computer (see column 9, lines 3-20).

With regard to claims 17, 27, Lupski teaches analysis of bacteria (see figure 11a).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hurst et al (Anal. Chem. (1998) 70:2693-2698) in view of Kohne et al (5,567,587).

Hurst teaches a method of claims 1 and 20 of identifying a bioagent in sample (see page 2696, column 1), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 2695, table I, and page 2694, column 2, where primers were synthesized which amplified a conservative region of the pmoA gene from methanotrophs and see figures 2-4 where molecular mass is shown for bioagents)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figure 4 and page 2696, where the MALDI-TOF can distinguish different microorganisms amplified by the 56 base pair regions).

With regard to claims 2, 4, 5, Hurst teaches environmental samples including groundwater and soil samples (see page 2693, column 1).

Hurst does not teach analysis of air samples.

Kohne teaches analysis of air sample for bacterial contamination (see column 40, lines 12-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect air samples as taught by Kohne for bacterial detection with the method of Hurst since Hurst expressly teaches bacterial detection of organism that are present in environmental samples and the legionella organism being

detected by Kohne is an important environmental pathogen that is present in air or water. An ordinary practitioner would have been motivated to modify the method of Hurst to analyze Legionella in air in order to determine whether this dangerous pathogen was present in a rapid and efficient way as Hurst notes "The methodology describe here has the potential to allow less expensive and faster characterization".

9. Claims 9,10 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurst et al (Anal. Chem. (1998) 70:2693-2698) in view of Romick et al (U.S. Patent 6,468,743).

Hurst teaches a method of claims 1 and 20 of identifying a bioagent in sample (see page 2696, column 1), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 2695, table I, and page 2694, column 2, where primers were synthesized which amplified a conservative region of the pmoA gene from methanotrophs and see figures 2-4 where molecular mass is shown for bioagents)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figure 4 and page 2696, where the MALDI-TOF can distinguish different microorganisms amplified by the 56 base pair regions).

With regard to claims 2, 4, 5, Hurst teaches environmental samples including groundwater and soil samples (see page 2693, column 1).

Hurst does not teach analysis of cosmetics, food or molds.

Romick teaches analysis of cosmetic and food samples for bacterial contamination (see column 23, lines 51-65). Romick also teaches detection of molds (see column 7, line 40).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze cosmetics and food for bacterial or mold detection as taught by Romick with the method of Hurst since Hurst expressly teaches bacterial detection of organism that are present in environmental samples and the organisms being detected by Romick are important contaminants of food and cosmetics. An ordinary practitioner would have been motivated to modify the method of Hurst to analyze bacteria or mold in food or cosmetics in order to determine whether dangerous pathogens are present in a rapid and efficient way as Hurst notes "The methodology describe here has the potential to allow less expensive and faster characterization".

10. Claims 12, 13, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Koster (WO 98/20166).

Muddiman teaches a method of claims 1 and 20 of identifying a bioagent in a sample (see abstract), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 3707, column 1, where the are

drawn to the 16S and 23S rRNA sequences, which are variable at some level at those locations and page 3707, column 2)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figures 2,-5 where the masses of two different species are compared).

With regard to claims 6 and 7, Muddiman teaches samples in a container in a building (see page 3707, column 1).

With regard to claim 11, 21, Muddiman teaches analysis of separate PCRs followed by comparison of the results (see figures 2-5) which comparison necessarily utilized a computer database that stored the spectra and generated figure 2, and where the data was stored in the computer database.

With regard to claims 14-15, 24, 25, Muddiman uses FT-ICR mass spectrometry with ESI (see page 3707, column 2).

With regard to claims 16, 26, the spectra of Muddiman show the presence or absence of the organisms, which provides some measurement of quantity (see figures 2-5).

With regard to claim 17, 27, Muddiman teaches that the bioagent is a Bacilli bacterium (see abstract).

Muddiman teaches using FT-ICR-MS to analyze and compare the PCR products but does not teach base composition signatures.

Koster teaches a method for detecting a single nucleotide polymorphism in an individual using molecular mass measurements such as MALDI TOF (page 14, for example), by determining the molecular mass of said amplification product using mass spectroscopy (page 13, line 1 and page 157, lines 10-29 and example 19) and comparing the molecular mass to the molecular mass of said region in an individual known to have said polymorphism, where if said molecular masses are the same then said individual has said polymorphism (page 13, lines 2-5 and page 158, lines 1-29, where Koster expressly compares patient 1 to a negative control and example 19).

With regard to claims 12, 13, 22 and 23, Koster expressly teaches comparison of base compositions with both modified and unmodified products (see page 66, for example, as well as page 105, table II and pages 69-70). At page 105, table II, Koster provides the base composition of three different PCR products determined by MALDI-TOF. Further, Koster specifically discusses using base composition to analyze mutations as discussed on page 70, where Koster notes "MS can also be used to determined full or partial sequences of larger DNAs; this can be used to detect, locate, and identify new mutations in a given gene region."

In particular, Koster expressly teaches the use of MALDI-TOF for diagnosis of bacterial or viral infections (see pages 73-79). Koster exemplifies this analysis in Example 5.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry method of Koster in the analytical method of Muddiman since Koster states "In another embodiment, an accurate sequence determination of a relatively large target nucleic acid, can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments to determine the sequence of the larger target nucleic acid (see page 75, line 26 to page 76, line 2)." So an ordinary practitioner would have been motivated to detect the PCR products of Muddiman with the base composition Mass spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

11. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hurst et al (Anal. Chem. (1998) 70:2693-2698) in view of Romick et al (U.S. Patent 6,468,743) and further in view of Haugland et al (Mol. Cell. Probes. (1998) 12:387-396).

Hurst in view of Romick teach the limitations of claim 18 as discussed above. In particular, Romick teaches identification of molds.

Hurst in view of Romick do not teach identification of the specific molds of claim 19, including Stachybotrys.

Haugland teaches the use of PCR for detection of Stachybotrys.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze samples for mold detection as taught by

Romick for the specific toxic fungal species of Stachybotrys with the method of Hurst since Hurst expressly teaches bacterial detection of organism that are present in environmental samples. An ordinary practitioner would have been motivated to modify the method of Hurst to analyze mold such as Stachybotrys in order to determine whether dangerous pathogens are present in a rapid and efficient way as Hurst notes "The methodology describe here has the potential to allow less expensive and faster characterization". The ordinary practitioner would have been motivated to analyze for Stachybotrys by Haugland, who notes that this organism causes human illness as well as contamination of animal feedstocks (see pages 387-388).

Double Patenting

12. Claims 1-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 59,60,62,63,66,69-76 and 79-94 of copending Application No. 10/156,608. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/660,997 in view of Muddiman. Although the conflicting

claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific biowarfare organisms are selected. Muddiman teaches selection of Bacillus including bacillus anthracis. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of claims 1-28 of copending Application No. 10/660,997 with Muddiman in order to detect organisms of interest such as Anthrax.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Given the large number of related cases which show up on PALM, many of which are abandoned, Applicant is requested to comply with 37 CFR 1.56 by identification of

copending applications, particularly applications close to issuance, which raise double patenting issues.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
2/17/06